



## REM Sleep behavior disorder in Parkinson's disease: a model for identification and prediction of its progression from the prodromal stage

Cesari, M.; Christensen, J.A.E.; Sørensen, H.B.D.; Mollenhauer, B.; Muntean, M.-L.; Trenkwalder, C.; Sixel-Döring, F.; Jennum, P.

*Published in:*  
Sleep Medicine

*Link to article, DOI:*  
[10.1016/j.sleep.2019.11.164](https://doi.org/10.1016/j.sleep.2019.11.164)

*Publication date:*  
2019

*Document Version*  
Peer reviewed version

[Link back to DTU Orbit](#)

### *Citation (APA):*

Cesari, M., Christensen, J. A. E., Sørensen, H. B. D., Mollenhauer, B., Muntean, M.-L., Trenkwalder, C., Sixel-Döring, F., & Jennum, P. (2019). REM Sleep behavior disorder in Parkinson's disease: a model for identification and prediction of its progression from the prodromal stage. *Sleep Medicine*, 64, S59-S60. <https://doi.org/10.1016/j.sleep.2019.11.164>

---

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

# REM Sleep behavior disorder in Parkinson's disease: a model for identification and prediction of its progression from the prodromal stage

M.Cesari<sup>1</sup>, J.A.E.Christensen<sup>1,2</sup>, H.B.D.Sorensen<sup>1</sup>, B.Mollenhauer<sup>3,4</sup>,  
M.-L.Muntean<sup>4</sup>, C.Trenkwalder<sup>4</sup>, F.Sixel-Döring<sup>4,5</sup>, P.Jennum<sup>2</sup>

<sup>1</sup>Department of Health Technology, Technical University of Denmark, Kgs. Lyngby, Denmark  
<sup>2</sup>Danish Center for Sleep Medicine, Department of Clinical Neurophysiology, Rigshospitalet, Glostrup, Denmark

<sup>3</sup>University Medical Center, Goettingen, Germany

<sup>4</sup>Paracelsus-Elena-Klinik, Kassel, Germany

<sup>5</sup>Department of Neurology, Philipps University, Marburg, Germany

**Introduction:** Around 33-46% of Parkinson's disease (PD) patients have REM sleep behavior disorder (RBD), and evidence suggests that REM behavioral events (RBEs) are a prodromal stage of RBD. Few studies have investigated other electrophysiological changes other than REM sleep without atonia in PD patients with RBD. This work has two aims: 1) to develop a data-driven model that, based on sleep electroencephalogram (EEG) and electrooculogram (EOG), can identify RBD in PD patients; and 2) to apply the developed model to PD patients with RBEs to evaluate its ability to predict their progression to full-blown RBD.

**Materials and methods:** We analyzed video-polysomnography (v-PSG) data in a baseline study of 107 *de novo* PD patients, of whom 54 had normal REM sleep (PDnonRBD), 27 had RBEs (PD+RBE) and 26 had definite RBD (PD+RBD). The patients were re-evaluated with v-PSG at 2-year follow-up (FU).

We included C3-A2, C4-A1 EEG and LOC-A2, ROC-A1 EOG signals in our analysis. We first applied a validated automated macro-sleep (30-s epochs) and micro-sleep (5-s mini-epochs) staging algorithm. Features describing micro-sleep structure, as well as features describing EEG spectral content, EEG complexity, EEG coherence and EOG time-frequency energy were extracted. All the features were given in input to a machine learning system consisting of an ensemble of random forest classifiers, giving as outputs the probabilities of having RBD or not ( $P(\text{RBD})$  and  $P(\text{nonRBD})$  respectively). A participant was classified as having RBD if  $P(\text{RBD})$  exceeded  $P(\text{nonRBD})$ .

The developed system was applied to PDnonRBD and PD+RBD groups to evaluate accuracy, sensitivity and specificity of RBD identification and we identified the features that mainly contributed to a successful RBD detection. Then, it was applied to PD+RBE patients and we evaluated with receiver operating characteristic analysis whether  $P(\text{RBD})$  could distinguish the 9 participants that developed full-blown RBD at FU from the other 16 ones that did not.

**Results:** RBD could be detected with accuracy, sensitivity and specificity over 80%. Features describing micro-sleep structure played a major role in correct identification of RBD and we observed that PD+RBD patients were characterized by increased wake-sleep transitions, REM fragmentation and REM instability compared to PDnonRBD. PD+RBE patients that developed RBD at FU study showed significantly higher  $P(\text{RBD})$  and could be differentiated from the ones that did not (area under the receiver operating curve of 0.87, sensitivity of 77.8% and specificity of 87.5%).

**Conclusions:** We developed a data-driven model able to identify RBD from EEG and EOG and to predict progression from RBEs to definite RBD in PD patients. The increased micro-sleep instability in PD+RBD might suggest dysfunction of sleep-wake

regulation in PD with RBD and support the hypothesis that PD+RBD patients have more severe neurodegeneration. The results further confirm RBEs as prodromal stage of RBD and, as micro-sleep instability has high importance in identification of RBD, micro-sleep instability might be considered as a biomarker for progression from the prodromal stage of RBD to full-blown RBD in PD patients.